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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,464	ADLER ET AL.	
	Examiner	Art Unit	
	Zachary C Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *4-15 and 27-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/5/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-67 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1-3 and 16-26, in the reply filed on 12/10/2004 is acknowledged.

The traversal is in part on the ground(s) that a search of both Group I and Group III, drawn to T2R76 polypeptides, would be co-extensive. This is not found persuasive because consistent with current practice, a serious search burden may be established by (A) separate classification thereof; (B) a separate status in the art when they are classifiable together; or (C) a different field of search. These criteria were met in the above restriction. As stated in the MPEP § 803, "a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02." Further, a search is directed not only to art that would be anticipatory, but also to art that would render the invention obvious. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4-15 and 27-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3 and 16-26 are under consideration.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The current title is "Identification of a novel bitter taste receptor" whereas the claims are directed to T2R76 nucleic acids and systems for expression.

The disclosure is objected to because of the following informalities:

1) Paragraph 33 of the specification contains three instances where underlined blanks are present, e.g. "_____". These should be replaced with the appropriate text.

2) Paragraph 33 refers to US Patent Application 20020094502, by Adler, Jon Elliot, published July 18, 2002. However, US Patent Application publication 20020094502 has different inventors and a different publication date. It is believed that Applicant meant to refer to US Patent Application publication 20020094551, which lists the inventor Jon Adler Elliot and was published July 18, 2002.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-3 and 16-26 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are directed to polynucleotides of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO: 2, termed T2R76, wherein the polypeptide is believed to be a component of a taste transduction pathway, particularly bitter taste transduction

(paragraph 5, page 3), yet the specification has not taught how to use this information in any particular way. The concept of "bitter taste" is known to involve multiple and as yet poorly characterized transduction schemes, see for example Perruccio et al, Society for Neuroscience Abstracts 26(1-2) Abstract No. 66.15, 2000 (cited on the IDS submitted by Applicant 2/5/2004). These transduction schemes are also thought to involve a large diversity of receptors – each receptor thought to bind specifically among a tremendous genus of structurally unrelated toxic or bitter tasting compounds, see the Abstract of Chandrashekar et al., Cell 100(703-711) 2000 for example (cited on the IDS submitted by Applicant 2/5/2004). The specification has given no indication as to which of these compounds is expected to bind to and activate SEQ ID NO: 2. Without such knowledge, the artisan could not use the protein to manipulate any aspect of the senses involving taste. Instead, the specification has merely invited the skilled artisan to embark on a plan of research to try to find exactly what ligands to use and then to determine what the protein can be used for.

The instant specification (paragraphs 3-5, pgs 1-3) puts forth the instant T2R76 is a member of the T2R family of taste-cell-specific GPCRs as described in Chandrashekar et al., Cell 100(703-711) 2000; and that such family members are believed to be involved in the taste detection of bitter substances. The specification further puts forth that the polypeptides are useful for screening for "T2R76 modulators that can be developed as additives to alter taste of a composition for oral use, including but not limited to food, beverages, oral washes, dentifrices, cosmetics, and pharmaceuticals, as described further herein below...for example, an inhibitor of T2R76 can be used to reduce bitter taste" (paragraph 127, pgs 46-47), although the specification does not appear to assert that the instant polypeptide mediates a response to any particular tastant or ligand. This proposed uses lacks a substantial utility, because it is of a general nature, and it would require undue experimentation on the part of the skilled artisan to determine for what, particularly, the claimed polynucleotides could be used.

A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out

further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material that has a stated correlation to a predisposition to the onset of a particular disease would be a practical use of the material. However, a method of modulating an unidentified aspect of what is collectively known as taste perception with an as yet unidentified material (e.g. agonists of the disclosed polypeptides) would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

A stated belief that a correlation exists between the polypeptides and any of the collective phenomena that are encompassed by the concept of taste perception is not sufficient guidance to use the claimed polynucleotides to modulate any aspect of taste perception; it merely defines a starting point for further research and investigation and presents only an invitation to one of skill in the art to perform such further research and investigation. The molecular mechanisms of taste perception are extremely complex and are known to use multiple transduction mechanisms. Even what could be thought of as a singular modality of taste perception, e.g. the perception of bitter taste, is not a single modality but a generalized response that is known to involve multiple and as yet poorly characterized transduction schemes, see for example Perruccio et al, Society for Neuroscience Abstracts 26(1-2) Abstract No. 66.15, 2000. Thus, the asserted uses of the polynucleotides as they relate to taste perception, are general and do not assert any particular use beyond an invitation to the skilled artisan to try to find a particular way in which the polynucleotides or polypeptides could be used.

Further, the asserted membership of the instant polypeptide in the family of T2R proteins described by Chandrashekar et al., (supra) does not, alone, impart a property to the polypeptide that could be exploited in such a way as to constitute a substantial utility. Chandrashekar et al. tested 11 different human T2R clones against a battery of different tastants and found only one clone that responded - and this response seems to be limited to only one tastant (see col 1 of page 707 and List of Tastants at page 710). Further, even this success seems to be rare in the art. Commenting on this family of receptors, other researchers have concluded that although T2R receptors have been

suggested to be candidates for bitter taste receptors, "at present there is no functional evidence for this proposal", see Lindemann, B. Nature Neuroscience 3(2)99-100, 2000, last paragraph of column 2 of page 99 (cited on the IDS submitted by Applicant 2/5/2004). Applicant's disclosure simply offers an additional object for the skilled artisan to examine. Although Applicant's disclosure would be immediately recognized as presenting an exciting research opportunity, a product whose only asserted utility is as an object of such research is not patentable under 35 U.S.C. § 101.

The specification puts forth (paragraph 81, pages 31-32) that the nucleic acid molecules can be "used to detect T2R76 gene variants or altered expression. For example, detection of a change in T2R76 sequence or expression can be used for diagnosis of T2R76-related differences in taste perception". While one of skill in the art would appreciate that polymorphisms in the disclosed sequences, or variations in the expression of the polynucleotide, must exist in any large population, this amounts to nothing more than an invitation to the skilled artisan to try and find such polymorphisms or altered expression. Moreover, the specification does not teach that any particular nucleic acid or amino acid sequence, or level of expression, is distinctive of any individual nor of any particular phenotype, e.g. the specification does not assert that a mutation in the gene, or alteration in expression, would affect the ability to perceive any particular bitter tastant – or bitter taste in general.

Thus, the instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

Therefore, since the polypeptides of the invention are not supported by a specific and substantial utility, or a well-established utility, the encoding polynucleotides, as well as the heterologous systems of expression of the polypeptide, also lack utility.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3 and 16-26 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a substantial asserted utility, for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Additionally, should a specific or substantial utility be established for the claims, claims 1, 2, 16-18 and 20-26 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, which would then be enabling for a polynucleotide of SEQ ID NO: 1 and a polynucleotide encoding a polypeptide of SEQ ID NO: 2, and systems of expression comprising isolated host cells comprising these polynucleotides, does not reasonably provide enablement for 1) polynucleotides that are "substantially similar" to SEQ ID NO: 1, 2) variants and fragments of SEQ ID NO: 1 that hybridize to SEQ ID NO: 1, or 3) polynucleotides with one or more changes to the sequence of SEQ ID NO: 1, or 4) systems of expression comprising host cells in an organism or 5) systems of expression comprising a nucleotide encoding a T2R other than a human T2R. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, 16-18, and 20-26 encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 2, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 2 or comprising only portions of SEQ ID NO: 2. Claim 1 encompasses polynucleotides "substantially similar" to SEQ ID NO: 1, and while it is unclear what the metes and bounds of this phrase are (see the 112, 2nd rejection below), the term as written is broad enough to encompass a polynucleotide encoding a polypeptide with any number of variations to SEQ ID NO: 2. Claims 2, 18,

and 20-26 encompass a nucleic acid that hybridizes to SEQ ID NO: 1, including nucleic acid fragments, with one or more changes to the codons, that encode polypeptide fragments with one or more changes to the protein sequence. Claim 16 encompasses all "T2R76" polypeptides, which are not limited to a sequence of SEQ ID NO: 2, and therefore encompasses polypeptides with one or more changes to the sequence of SEQ ID NO: 2. Claim 17 encompasses polypeptides that are "substantially identical" to SEQ ID NO: 2, and polypeptides encoded by polynucleotides that are "substantially identical" to SEQ ID NO: 1. The term "substantially identical" is given two different definitions in the specification: on page 13, paragraph 36, it is defined as 60% or greater similarity between two sequences, and on page 27, paragraph 72 it is taught "The term "substantially identical" also encompasses polypeptides that are biologically functional equivalents of a T2R polypeptide, e.g. T2R76 polypeptide."

Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 2, but which still retain a desired property of the polypeptide of SEQ ID NO: 2. The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, Applicant has not provided guidance as to what properties of sequence or allelic variants of the protein corresponding to SEQ ID NO: 2 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 2 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 2 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 2, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 2.

The specification has failed to provide an activity of SEQ ID NO: 2 to be used to evaluate the claimed variants for usefulness, e.g. no particular ligand has been disclosed to bind and activate the protein, so the artisan would not know how to test variants for functionality. The specification has not provided a working example of a

usable variant of the polypeptide of SEQ ID NO: 2, nor sufficient guidance so as to enable one of skill in the art to make such a variant.

The problem of predicting protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; cited on the IDS submitted by Applicant 2/5/2004). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89 (3352-3356) 1992; cited on the IDS submitted by Applicant 2/5/2004). Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 2 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

The problem of producing active variants appears especially difficult in the art of T2R receptors, to which the instant polypeptide is asserted to belong. The instant specification appears to simply suggest to the artisan that art-recognized procedures for screening GPCRs (e.g. paragraph 152, pg 57) are sufficient to identify functional variants of SEQ ID NO: 2. However, Hoon et al., Cell 96 (541-551) 1999 (cited on the IDS submitted by Applicant 2/5/2004), report that "We have attempted to determine the ligand/tastant specificity of TR1 and TR2 using a variety of strategies but have been hampered by the difficulty of functionally expressing these molecules in heterologous systems" see col 1 of page 547. Further, Chandrashekar et al. reported that they were able to record a response from only 1 of the 11 human T2R clones tested, see col 1 of page 707, and see above. Thus, the art regarding T2R receptors, as exemplified by Hoon et al., Chandrashekar et al, and Lindemann (discussed above), recognizes the complexity, unpredictability, and non-routine nature of the work involved in trying to assay functional T2R receptors. The instant specification has provided only general guidance to the skilled artisan - such guidance does not supply the artisan with the detailed methods one would need to possess in order to screen for functional variants. Further, the specification has offered no working example of such a screening method.

The specification has also failed to teach where to look for naturally occurring allelic variants of SEQ ID NO: 1, e.g. no disorder or phenotype has been asserted to correlate with a naturally occurring allelic variant, such that the artisan might now where to obtain a variant. The specification merely offers the skilled artisan the invitation to randomly try to find variants through trial and error sampling of animal populations.

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and the difficulties encountered in screening T2Rs, exemplified by Hoon et al., Chandrashekar et al., and Lindemann, and the breadth of the claims which fail to recite adequate

structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope should a substantial utility be established for the claimed polynucleotides.

Claims 16-26 are drawn to systems of expression comprising host cells comprising a polynucleotide encoding a T2R76, and encompass both isolated host cells and host cells within an organism, such as would be used in gene therapy. The specification on page 33-35 teaches systems of expression of T2R76 and Examples 2 and 3 on pages 70-71 discuss expression of T2R76. All of the teachings in the specification are directed to isolated host cells; there are no examples directed towards systems of expression within an organism. It is acknowledged that the level of skill of those in the art is high, but it is not disclosed and not predictable from the limited teachings of the prior art and specification if the expression system of the present invention could be used for gene therapy. Thus the specification fails to teach the skilled artisan how to use host cells comprising the T2R76 polynucleotides for expression within an organism without resorting to undue experimentation. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use the host cells comprising the polynucleotide for the above stated purpose. Due to the large quantity of experimentation necessary to determine if the host cells comprising the T2R76 polynucleotide could be used for gene therapy, the lack of direction/guidance presented in the specification regarding same, lack of working examples and the limited teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention. What Applicant has provided is a mere wish or plan and an invitation to experiment to determine if the host cells comprising the T2R76 polynucleotide could be used within an organism for gene therapy.

Claim 20 is directed to a system of claim 18 further comprising a nucleotide encoding another T2R. This claim encompasses T2Rs from species other than humans. The specification provides a long list of human T2Rs that are known in the art on page 12. Although, the specification refers to mouse and rat sequences on page 13, the specification does not provide any specific examples of T2Rs from species other than

humans, or how to identify such sequences through structural features. In order to use the invention as claimed, the skilled artisan would need to engage in undue experimentation in order to determine if T2R sequences from other species could be identified or not. Due to the large quantity of experimentation necessary to identify T2R sequences in species other than humans, the lack of direction/guidance in the specification regarding same, lack of working examples and limited teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skill artisan in order to use the claimed invention.

5. Claims 1, 2, 16-18, and 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polynucleotide of SEQ ID NO: 1, yet the claims encompass polynucleotides that are not described in the specification, e.g. mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polynucleotide, that of SEQ ID NO: 1, encoding a polypeptide with no instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial

portion of the genus. The instant specification discloses, however, a single isolated polynucleotide sequence SEQ ID NO: 1, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

The specification has not provided a particular essential feature, either a functional or structural feature, that the claimed genus of polynucleotides possesses. The recitation of the property of hybridization does not, alone, provide sufficient information regarding the structure of the claimed polynucleotide variants. Further, most of these variants are expected to encode polypeptides having an amino acid sequence different than that of SEQ ID NO: 2 and thus having different structural and functional properties. Similarly, the recitation of a percent identity to SEQ ID NO: 2 provides no description of any amino acid sequence other that of SEQ ID NO: 2. The specification has not defined what particular common structural or functional properties are possessed by the claimed genus of polynucleotides. Thus one of skill in the art would appreciate that Applicant was not in possession of the claimed genus of polynucleotides at the time of filing.

The instant claims are not directed to that which is disclosed as essential to the invention, i.e. something that is homologous to the parent SEQ ID NO: 1 and has the function of the parent polynucleotide. Thus, with the exception of the polynucleotide of SEQ ID NO: 1, and other polynucleotides which encode a polypeptide of SEQ ID NO: 2, the skilled artisan cannot envision encompassed variants. Therefore, only a polynucleotides encoding a polypeptide of SEQ ID NO: 2, and polynucleotides consisting of fragments thereof, or polynucleotides consisting of fragments thereof and heterologous sequences (e.g. carrier or tag sequences), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim 20 also lacks written description because the claims encompass T2R nucleic acids of species other than humans, but the specification only provides examples of human T2Rs that are known in the art (page 12). Furthermore, the specification does not teach what features the claimed genus of T2R polynucleotides must possess. Thus one of skill in the art would appreciate that Applicant was not in possession of the claimed genus of T2R polynucleotides at the time of filing.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3 and 16-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially similar" in claim 1 is a relative term which renders the claim indefinite. The term "substantially similar" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification defines the term "substantially identical" on page 13, paragraph 36, but does not provide a definition for the term "substantially similar". Because the term "substantially similar" is different than the term "substantially identical", it is assumed that a different meaning is intended, but no definition is supplied for the term and therefore the metes and bounds of the term are unclear.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a heterologous nucleic acid encoding the T2R76 polypeptide. The claim is drawn to a system for heterologous expression comprising a host cell expressing a T2R76 polypeptide. In order for a host cell to express a heterologous polypeptide, the host cell must contain a heterologous nucleic acid.

Claim 18 is indefinite because it is unclear how the polypeptide of claim 17, from which claim 18 depends, is meant to comprise another polypeptide, as claim 18 is directed to. For examples, if claim 17 comprises a polypeptide of SEQ ID NO: 2, it is unclear how the polypeptide of claim 18 is meant to further comprise a polypeptide

encoded by SEQ ID NO: 1. While this could be done in the art (e.g., a fusion protein), it isn't understood if, for example, the 2nd polypeptide is inserted into the middle of the T2R76 polypeptide, if this is still considered a T2R76 as stated in claim 16.

Claims 21 and 22 are indefinite because it is unclear how one cell (e.g., host) can comprise another cell (e.g., mammalian).

The remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1-3 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by WO200257309-A1, Miwa et al, published July 25, 2002.

Miwa et al teaches (page 90) a 954 residue nucleic acid sequence (SEQ ID NO: 2) that is 99.6% similar to SEQ ID NO: 1 of the instant application. An alignment of these two sequences is attached to this Office Action (see Attachment #1). As indicated in the Abstract provided in Attachment #1, this sequence encodes a novel G-protein coupled receptor protein. SEQ ID NO: 1 of the instant application is 957 nucleotides in length. The sequence taught by Miwa is 954 nucleotides length and is missing the last 3 nucleotides as taught by SEQ ID NO: 1 of the instant application. The alignment indicates there is 1 conservative mismatch at position 930 of each sequence; however, at this position in SEQ ID NO: 1 of the instant application is a Y nucleotide residue, which indicates a this position can be any pyrimidines (e.g. either a C or T), and Miwa at position 930 has a C.

The instant application does not clearly define "substantially similar", but does provide a definition of the term "substantially identical" on page 13, where it is defined

as any sequences that share 60% or greater sequence identity. Therefore, SEQ ID NO: 2 taught by Miwa is substantially similar to SEQ ID NO: 1 of the instant application, as recited in part (c) of claim 1. SEQ ID NO: 2 of Miwa is a double-stranded DNA molecule, and therefore includes a complementary strand that could hybridize to a nucleic acid sequence of SEQ ID NO: 1 of the instant application under stringent conditions such as part (c) and (d) of claim 2.

Miwa further teaches (pages 88-90) an amino acid sequence, SEQ ID NO: 1, that is encoded by the nucleic acid sequence SEQ ID NO: 2. The amino acid sequence SEQ ID NO: 1 taught by Miwa is 100% identical to SEQ ID NO: 2 of the instant application. Therefore, nucleic acid sequence SEQ ID NO: 2 taught by Miwa encodes a protein of SEQ ID NO: 2 of the instant application, as recited in part (a) of each of claims 1-3.

Miwa does not teach that SEQ ID NO: 1 is a T2R76 bitter taste receptor; however, since sequence SEQ ID NO: 1 taught by Miwa is 100% similar to the amino acid sequence of SEQ ID NO: 2 of the instant application, SEQ ID NO: 1 taught by Miwa is being considered a T2R76 unless applicant provides evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO200257309-A1, Miwa et al, published July 25, 2002 in view of U.S. Patent No. 5,763,218, Fujii et al, published June 9, 1998.

The teachings of Miwa are summarized above. Miwa does not teach expression of the novel GPCR encoded by SEQ ID NO: 2 in a heterologous system.

Fujii teaches a nucleic acid encoding a novel human GPCR. Fujii further teaches (column 10, lines 25-32) "Various mammalian cell culture systems can also be employed to express recombinant protein...Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts...and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHOHS293, HeLa and BHK cell lines." Therefore, Fujii teaches a system for heterologous expression of a novel GPCR in mammalian cell lines, including human cell lines.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the heterologous expression systems as taught by Fujii to the novel GPCR encoded by SEQ ID NO: 2 as taught by Miwa. The person of ordinary skill in the art would be motivated to do so because Fujii teaches (in column 3) that the expressed GPCR protein can be used for further experimentation to screen for modulators of the GPCR function. The person of ordinary skill in the art would have expected success because Fujii teaches all of the techniques necessary to express a novel GPCR, and in the absence of other evidence, these techniques would be expected to work as well with the novel GPCR taught by Miwa as with the novel GPCR taught by Fujii.

The further limitation of claim 20 that the system further comprises a nucleic acid encoding another T2R is met by teaching of Fujii regarding the use of HeLa host cells (noted above). HeLa host cells are human cells that contain the entire human genome, and thus comprise all of the other genes that encode other T2R proteins.

Claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO200257309-A1, Miwa et al, published July 25, 2002 in view of U.S. Patent No. 5,763,218, Fujii et al, published June 9, 1998 and in further view of U.S. Patent No. 6,004,808, Negulescu et al, published 12/21/1999.

The teachings of Miwa are summarized above. Miwa does not teach expression of the novel GPCR encoded by SEQ ID NO: 2 in a heterologous system.

The teachings of Fujii are summarized above. Fujii does not teach expression of a novel GPCR in a host cell further comprising a promiscuous G protein alpha subunit, such as Gα15.

Negulescu teaches (col 2, lines 14-25) "the invention provides for the first time, a stable, isolated cell that expresses, from a construct, a Gα subunit of a promiscuous G-protein (e.g., Gα15 or Gα16)...these cells allow occupation of any G-protein coupled receptor (GPCR) by a ligand to be detected using a signal transduction detection system". Negulescu further teaches (col 12, lines 17-36) "many embodiments of the invention will include a polynucleotide encoding a GPCR not naturally occurring in the cell and a promiscuous Gα protein construct...The GPCR may be a GPCR of known function or of [sic] protein of unknown function, such as an orphan GPCR."

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the heterologous expression systems as taught by Fujii to the novel GPCR encoded by SEQ ID NO: 2 as taught by Miwa, and to use a host cell further comprising a Gα15 subunit, such as Gα15, as taught by Negulescu. The person of ordinary skill in the art would be motivated to do so because Miwa teaches a novel GPCR and Negulescu teaches that their method is applicable to any GPCR of unknown function. The person of ordinary skill in the art would have expected success because Fujii and Negulescu teach all of the techniques necessary to express a novel GPCR with a Gα15 protein, and in the absence of other evidence, these techniques would be expected to work as well with the novel GPCR taught by Miwa as any other novel GPCR.

Statement on prior art

It is noted that it would not be obvious over the prior art to include transducin or gustducin in the system of expression of a novel GPCR as taught by Fujii et al, for a novel GPCR as taught by Miwa, et al. Transducin and gustducin have been found to associate with T2R receptors in taste receptors, but not with novel G proteins in

general. Therefore, since Miwa does not teach that the novel GPCR sequence SEQ ID NO: 2 is T2R, it would not be obvious to express the novel GPCR sequence in a heterologous host cell further comprising transducing or gastducin.

Art of Note

9. The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon for a rejection are considered pertinent to the instant application:

a. WO 02/068579 (published 6 September 2002) Venter et al. Sequence 24358 teaches a sequence that shares 100% identity with SEQ ID NO: 1 of the instant application (see Attachment #2). WO 02/068579 claims priority to 10 January 2001, but is not prior art under 35 U.S.C. § 102(e) because it does not designate the US.

b. Conte et al, 2002 "Identification and characterization of human taste receptor genes belonging to the TAS2R family", Cytogenetic and Genome Research 98: 45-53. Conte teaches the amino acid sequence of a bitter taste receptor, T2R60, that is 100% identical to SEQ ID NO: 2 of the instant application. Conte et al, 2002, is not prior art because the publication date of Conte is after the priority date of the instant application.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER